involving a bifurcation site, restenotic lesions (including in-stent restenosis), two-vessel disease (a maximum of 2 lesions located in 2 different epicardial vessels), long lesions (up to 53 mm).

Methods: The primary endpoint of the study is the Target Lesion Revascularization (TLR) rate at 180 days after stent implantation. Secondary endpoints are Target Vessel Failure (TVF) at 180-days, Major Cardiac Events (MACE) at 30-days and 180-days, MACE at 1-year, 2-years and 3-years in a subset of 500 patients, device success, procedure success and resource utilization.

Results: As of abstract submission, data about 1252 patients enrolled at 80 investigational sites is available for analysis, for a total of 1435 lesions treated. Among these, 374 (34%) were restenotic lesions.

Conclusions: The patient recruitment in the DELIVER II study was completed on 9th of September 2002. Thirty-day safety results from the restenotic lesions subgroup will be available for presentation and will be compared with the outcome of other lesion subgroups. Multivariate analysis combining restenosis with other complicating factors will be presented as well.

* Manufactured by Cook Incorporated. DELIVER II is conducted by Guidant Corporation on behalf of Cook Incorporated.

1198-182 Oral Rapamycin for the Prevention of In-Stent Restenosis

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Background: Rapamycin, a macrolide antibiotic, inhibits SMC proliferation *in vitro and in vivo* by blocking cell cycle progression at the G1/S transition. Given the anti-proliferative and anti-migratory properties of rapamycin, it may have anti-restenosis properties after PTCA and placement of coronary stents. Recently, implantation of rapamycin (sirolimus) eluting stents in de novo lesions was shown to be safe and effective in inhibiting neointimal formation. The safety and efficacy of oral rapamycin in reducing the incidence of intimal hyperplasia and restenosis is not known.

Methods: Thirty Patients with stable exertional angina will receive standard therapy (ASA + Clopidegrol) plus rapamycin (loading dose 6 mg on the day of the procedure, followed by 2 mg/day) for either 2 (phase 1, n=15) or 4 (phase II, n=15) weeks after stent implantation for denovo lesions. Blood will be obtained for rapamycin levels, CBC, renal function and lipid profile. Quantitative coronary angiography (QCA) and IVUS imaging will be performed immediately after the procedure and at a 6 month follow-up in all patients for evaluation of the primary endpoint of neointimal volume and binary restenosis. **Results:** To date, 15 (completed study-phase one) patients (mean age 60±10, 70% males, 27% diabetics, 40% prior MI) have been enrolled. All patients tolerated the loading dose plus two week course of oral Rapamycin without any significant side effects or laboratory abnormalities. There was one episode of recurrent in-hospital ischemia (few hours after the procedure) for suboptimal angiographic result which required further stenting. Angiographic and IVUS follow-up is in progress and will be presented for these patients as well as the full safety data on all 30 patients.

1198-183 Oral Rapamune to Inhibit Restenosis in Patients With Multi De-Novo Coronary Lesions Requiring Stenting

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Background: Drug-eluting stents (utilizing antiproliferative agents such as Rapamune) have shown the ability to limit restenosis. Oral Rapamune (R) is an alternative delivery strategy that can target multi-stenosed coronary vessels and may potentially lower the cost and vessel toxicity.

Methods: The *O*ral *R*apamune to Inhi*bit* Restenosis (ORBIT) is an open label study of 60 patients (pts) with *de novo* coronary artery stenosis treated with stent implantation in up to 2 vessels. The first 30 pts received R 2 mg /day for 30 days, and the last 30 pts received R 5mg/day for 30 days. The loading dose for both regimens was 5 mg given either immediately prior to or after the intervention. Patients underwent clinical and angiographic follow-up.

Results: In the first 30 patients who received R 2 mg/day (age 60 ± 10 years, 86% males, 13.3% diabetes), the mean number of treated lesions per pt was 1.6 ± 0.5, with a reference vessel diameter of 3.0 ± 0.5 mm and mean lesion length of 19.7 ± 9.0 mm. Angiographic success was achieved in all pts. Mean pre-discharge serum R levels were 5.1 ± 3.1 ng/ml and at 30 days 6.5 ± 4.2 (17 pts). Drug therapy was discontinued in 3 pts from the 2 mg group and in 5 pts from the 5 mg group due to skin rash, diarrhea, mouth ulcers, or fatigue (or a combination of these symptoms). There were no biological or biochemical adverse affects.

In the 2 mg group, 49 lesions were treated. Of these, 40 were available for angiographic follow-up. The binary restenosis for in-stent was 5.0% and for in-segment was 7.5%. The late loss in-stent was 0.62 ± 0.61 and the in-segment was 0.29 ± 0.52 mm. Target lesion and vessel revascularization was 15.6%. **Conclusions:** Oral Rapamune administration for the prevention of restenosis is safe and feasible. Low rates of restenosis and late loss were observed with a dose of 2 mg/day. Complete 6-month follow-up for the R 5mg/d group will be available at presentation.

1198-184 Stent Release of a Rapamycin Analogue: Tissue Pharmacokinetics of Rapid Versus Delayed Release

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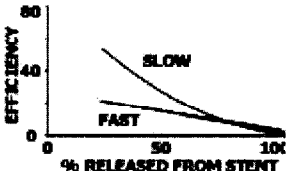
Background: The effect of drug release rates from stents on tissue uptake and biologic effect are poorly understood. We investigated tissue distribution under varied release conditions of a stent-delivered rapamycin analogue. **Methods and Results:** 38 rabbits underwent iliac artery stenting with a stent coated with a phosphorylcholine polymer loaded with ^{3}H drug (100 µg/stent). We compared 2 formulations; formulation 1- rapid release, and formulation 2- slow release. Animals were harvested at 1, 3, 7, 14, and 28 days and stent and tissue drug concentration determined through liquid scintillation counting. In vivo drug release from formulation 1 was >90% at 3 days. Release from formulation 2 did not reach >90% until 14 days(P=0.005 by ANOVA). Arterial deposition peaked at 1 day with formulation 1 (726.0±154.3 µg/g tissue) and at 3 days in formulation 2 (1339.0±412.8 µg/g tissue). When plotted against percent of drug released from stent, efficiency of deposition (µg drug/g tissue/µg drug released) from formulation 2 was best fit by a polynomial equation (R^2 0.64, p<0.001) and was greater (p=0.04 by ANOVA) than efficiency from formulation 1 which was best fit by a linear equation (R^2 0.58, p<0.001)(Figure). **Conclusion:** Delayed release enhances the efficiency of delivery of a rapamycin analogue to the vessel wall. Modulating release may offer a more effective method of enhancing stent-based drug delivery than increasing dose.



1198-185 Can Sirolimus-Eluting Stents Tolerate Some Degree of Geographic Miss?

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Background. Sirolimus-eluting stents have proven their ability to almost completely suppress 6-month neointimal proliferation in the stented segment. However, little is known on the efficacy in the segments adjacent to the stent, dilated but not stented.

Methods and Results. In a multicenter randomised bifurcation trial, between June 2001 and April 2002, 86 pts with a significant stenosis at a bifurcation were enrolled. The efficacy of sirolimus-eluting stents in these lesions has been evaluated. Pts were randomised into 2 groups of 43 each to receive either 2 stents (main vessel and branch) or 1 stent (main vessel only). At the operator's discretion 22 patients in the single stent arm have crossed over to the 2 stent arm. Baseline characteristics were comparable in both groups: mean age 63±10 years, males 80.2%, diabetes 22%, and unstable angina 17.4%.

By means of QCA, films of 47 pts were analyzed before and after intervention and at 6-months for the presence of geographic miss and its effect on restenosis. 5 patients who had acute procedural failure were excluded from the analysis. Geographic miss has been defined as any balloon inflation beyond the non-stented segment. The segments proximal and distal to the stent in the main vessel as well as the side branch have been examined for geographic miss.

Conclusion. Even in the era of drug-eluting stents, the process of restenosis is multifactorial and the presence of geographic miss does not seem to influence the restenosis rates in bifurcation lesions.

Study Group	Restenosis
No geographic miss (17/42)	6 (35%)
Geographic miss (25/42)	4 (16%)
Main vessel (10)	
Proximal to stent(4)	0
Distal to stent (6)	1
Side branch(19)	3

1198-186 Association Between Progression of Untreated Coronary Lesions and In-Stent Restenosis

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Background: Progression of coronary artery disease is not completely understood, neither for de-novo stenoses nor for in-stent restenosis (ISR) as accelerated arteriosclerosis. The objective of this angiographic study was to assess an association between presence of ISR and the progression of untreated coronary lesions.

Methods: A series of 212 high-grade native coronary stenoses (mean stenotic degree 88%) of 150 patients was treated by stent implantation; 129 additional lesions with mild to moderate stenoses (>30%) remained untreated. Quantitative coronary angiography analysis was performed after 6±2 months regarding ISR (stenosis >50%), coronary progression (increase in stenosis >20%) and regression (decrease >20%), resp. Angiographic, procedural and clinical characteristics were assessed for a possible association to ISR and/or coronary progression.

Results: ISR was seen in 83 of 212 (39%) stented lesions. Of predictive value were presence of diabetes mellitus (P=0.04) as well as cumulative time of inflations (P=0.01) as procedural determinants. Angiographic progression was found in 12 of 129 (9%) primarily untreated lesions. Progression of a normal segment or regression were not seen. Progression of native plaques was associated with presence of ISR in 11 cases and with absence of ISR in 1 case (P=0.01). Smoking (P=0.02) turned out predictive for plaque progression, whereas medication and procedural angiographic parameters did not. Notably, 9 of 11 (82%) patients with progression presented with acute coronary syndromes at follow-up.

Conclusion: The findings of the present pilot study show that restenosis of a target stenosis following stent implantation is associated with progression of other untreated lesions, and thereby suggest that both arteriosclerosis forms share common systemic pathogenic mechanisms. With presence of ISR, angiography of primarily untreated coronaries should be performed, especially in case of preexisting plaques.

POSTER SESSION

1199 Newer Devices for Percutaneous Interventions: Renal and Ilio Femoral Angioplasty

Tuesday, April 01, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 3:00 p.m.-4:00 p.m.

1199-173 Results of U.S. Phase I Clinical Trial of Closure of Patent Foramen Ovale Associated With Stroke/ Transient Ischemic Attack or Peripheral Embolism Using the Amplatzerfi Patent Foramen Ovale Device

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Background: Patients with a patent foramen ovale (PFO) and paradoxical embolism are at risk for recurrent thromboembolic events. We report the results of Phase 1 US clinical trial of patients who underwent transcatheter PFO closure for secondary prevention of paradoxical embolism using the Amplatzer® PFO occluder (APO).

Methods: From March 2000 through May 2002, 50 patients (28 males and 22 females) with PFO and at least 1 paradoxical embolic event were referred for transcatheter PFO closure using the APO. The median age was 41 yr. (range 15 – 61 yr.) and the median weight was 81 kg (range 45 – 118). Thirty-six patients had cryptogenic stroke, 10 patients had transient ischemic attack and 4 patients had peripheral embolism. Seventeen patients had both a PFO and an atrial septal aneurysm.

Results: Of 50 patients referred for closure, 49 underwent attempted closure of their PFO using the APO; one patient did not have a PFO. Fifty devices were successfully deployed in all 49 patients (one patient received two devices for two separate fenestrations). Immediate complete closure as documented by transesophageal echocardiography (TEE)"no passage of bubbles from right to left atrium during Valsalva" was achieved in 26/49 (53%) patients and at 24 hours, by transthoracic echocardiography (TTE) was achieved in 31 (63%) patients. The median fluoroscopy time was 10.5 minutes (range 2.8 – 43) and the median procedure time was 85.5 minutes (range 16 – 309). Complications encountered during and within the follow-up period included one patient who developed a hematoma and an AV fistula requiring surgery and two patients who developed atrial fibrillation. At 3-month follow-up, 44 patients had a TTE with contrast bubble study, 38 (86%) had complete closure. At a median follow-up interval of one year (range one month-569 days), there have been no recurrent embolic events.

Conclusion: Transcatheter closure of PFO using the APO seems to be a safe and effective therapy in the prevention of thromboembolic events in patients with a history of presumed paradoxical embolism.

1119-174 Results of U.S. Phase I and II Clinical Trials of Transcatheter Closure of Patent Ductus Arteriosus in Adult Patients Using the Amplatzerfi Duct Occlud

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Background: Surgical closure of patent ductus arteriosus (PDA) in adult patients may be problematic. Recently, transcatheter closure of PDA using the Amplatzer duct occluder (ADO) has been shown to be safe and efficacious. We present our experience with this device in the adult population.

Methods: Between January 2000 and January 2002, forty-one adult patients (31 females and 10 males) with a PDA were referred for closure with the ADO. The median age was 35.6 years (range 18 – 70.7). The median Qp/Qs was 1.4 (range 0.6 – 3.5). The median diameter of the pulmonary artery end (narrowest diameter) was 3.4 mm (range 1.5 – 10); the median diameter of the ampulla was 10.7 mm (range 3.0 – 32) and the median length was 10.8 mm (range 1.5 – 35). According to the Toronto classification, there were 33 Type A PDA's: 1 Type B; 1 Type C; 2 Type D and 4 Type.

Results: Of forty-one patients, thirty-seven underwent attempted closure of their PDA using the ADO. In the remaining four patients, the PDA was small, and was closed using Gianturco coils. The device was successfully deployed in all but one patient (the ductus could not be crossed and the patient ultimately had successful PDA closure using a Gianturco coil). Moderate sized devices were used more frequently (1 patient received the 5/4 device; 2 the 6/4; 22 the 8/6; 7 the 10/8; 3 the 12/10; 1 the 14/12 and 1 patient received the 16/14 mm device). Complete angiographic closure was seen immediately after device deployment in 29 out of 36 (81%) patients. At 24 hours, complete closure as evidenced by color Doppler echocardiography was demonstrated in 34 out of 36 (94%) patients. The remaining two patients had small residual shunt. At 6-month and 1-year follow-up, complete closure was demonstrated in 35 out of 36 (97%) patients. In the two patients with small residual shunts at 24 hours post-procedure, one patient demonstrated complete closure by echocardiography at 6-months post-procedure. The other patient had no available follow-up. No complications related to device implantation occurred in any patient.

Conclusions: Closure of PDA using the ADO is safe and effective in adult patients

1199-175 Predictors of Clinical Outcome in Patients Undergoing Peripheral Vascular Interventions: Insights From the University of Michigan Peripheral Vascular Disease Quality Improvement Initiative (PVD-QI2)

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BACKGROUND: Statins and anti-platelet therapy are beneficial in patients undergoing percutaneous coronary interventions. Minimal data exists on the effectiveness of statins and dual antiplatelet therapy in patients undergoing peripheral vascular interventions.

METHODS: 79 patients underwent peripheral vascular interventions between Jan 2001-Feb 2002. Clinical, procedure, and outcome data were collected by use of a standardized form and follow-up by structured phone call > 6 months post-procedure. Multivariate logistic regression analysis was used to adjust for baseline characteristics and comorbidities and adjusted odds ratios were calculated for the composite of death, MI and stroke at 6-months.

RESULTS: Fourteen of the 79 patients (17.7 %) had one or more clinical event (death, MI or stroke). After adjustment for demographics and comorbidities, statin therapy (OR=0.21, 95% CI 0.05 - 0.86, p=0.03) and clopidogrel therapy (OR=0.17, 95% CI 0.04 - 0.78, p=0.02) were associated with a significant reduction of the composite event rate at 6 months.

CONCLUSIONS: In this study cohort of patients undergoing peripheral endovascular intervention, statin therapy and anti-platelet therapy with clopidogrel were each associated with a significantly lower risk-adjusted cardiovascular event rate at six months follow-up. These preliminary findings offer logical targets for quality improvement.

Multivariate predictors of major adverse cardiac events after peripheral interventions

	No event (n=65)	Event (n=14)	Adjusted Odds ratio (95% CI)	P value
Age	66.8± 10.1	69.5 ± 11.4	1.02 (0.96-1.09)	0.41
Serum creatinine	1.2 ± 0.6	1.8 ± 0.8	2.27 (0.88-5.86)	0.08
Diabetes	29.6 %	35.7 %	1.80 (0.39-8.12)	0.40
Statin use	64.1 %	28.5 %	0.21 (0.05-0.86)	0.03*
Clopidogrel use	82.8 %	57.1 %	0.17 (0.04- 0.78)	0.02*

1199-176 Stenting of Renal Artery Stenosis Preserves Renal Function in Both Diabetic and Nondiabetic Patients With Chronic Renal Insufficiency

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Background: Renal artery stenting has been shown to stabilize or improve renal function in a significant proportion of patients with atherosclerotic renovascular disease and impaired renal function. Whether diabetic (DM) patients obtain similar benefits as nondiabetic patients (NDM) is unknown.

Methods: The renal function of 36 consecutive patients with bilateral renal artery stenoses (11 DM; 25 NDM) and renal insufficiency (serum creatinine >/= 1.5 mg/dl) was analyzed by plotting the reciprocal of serum creatinine versus time in days before and after stenting.

Results: All patients had deterioration of renal function prior to intervention. At 47.4 +/- 31.2 months post intervention, renal function improved or did not change in 76% and worsened in 24% of NDM patients compared to 73% and 27% of DM patients respectively (p=NS). (Figure)

Conclusion: Renal artery stenting is equally beneficial in DM and NDM patients with impaired renal function and atherosclerotic renal artery stenosis.